A riboswitch gives rise to multi-generational phenotypic heterogeneity in an auxotrophic bacterium

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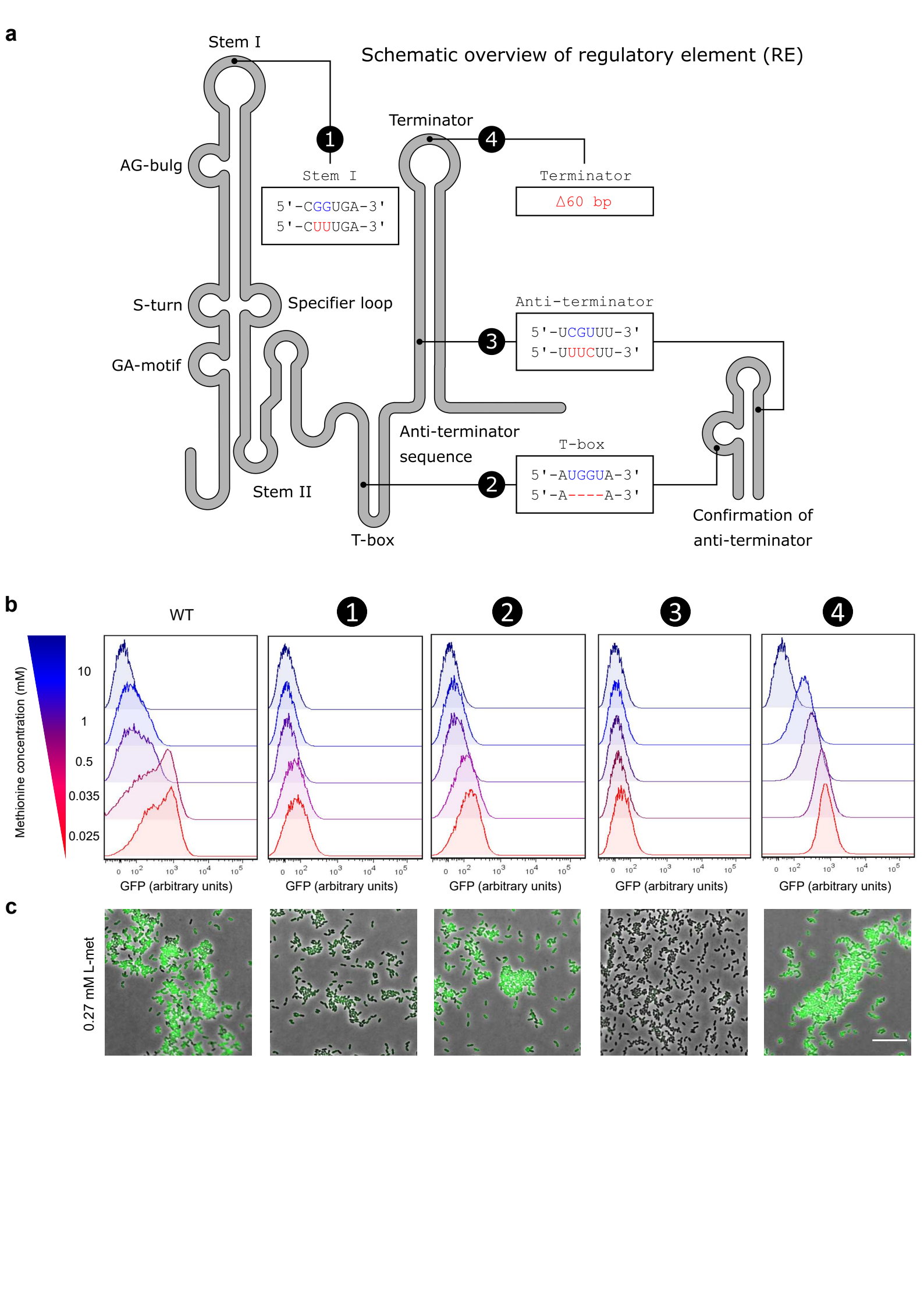
Abstract: Auxotrophy, the inability to produce an organic compound essential for growth, is widespread among bacteria. Auxotrophic bacteria rely on transporters to acquire these compounds from their environment. Here, we study the expression of both low- and high-affinity transporters of the costly amino acid methionine in an auxotrophic lactic acid bacterium, Lactococcus lactis. We show that the high-affinity transporter (Met-transporter) is heterogeneously expressed at low methionine concentrations, resulting in two isogenic subpopulations that sequester methionine in different ways: one subpopulation primarily relies on the high-affinity transporter (high expression of the Met-transporter) and the other subpopulation primarily relies on the low-affinity transporter (low expression of the Met-transporter). The phenotypic heterogeneity is remarkably stable, inherited for tens of generations, and apparent at the colony level. This heterogeneity results from a T-box riboswitch in the promoter region of the met operon encoding the high-affinity Met-transporter. We hypothesize that T-box riboswitches, which are commonly found in the Lactobacillales, may play as-yet unexplored roles in the predominantly auxotrophic lifestyle of these bacteria.

DOI: https://doi.org/10.1038/s41467-020-15017-1

Originally published at:
Hernandez-Valdes, Jhonatan A; van Gestel, Jordi; Kuipers, Oscar P (2020). A riboswitch gives rise to multi-generational phenotypic heterogeneity in an auxotrophic bacterium. Nature Communications, 11(1):1203.
DOI: https://doi.org/10.1038/s41467-020-15017-1


a
Schematic overview of regulatory element (RE)
Stem I
Terminator
AG-bulg
1
4
Stem I
5'-CGGUGA-3'
5'-CUUUGA-3'
Terminator
Δ60 bp
S-turn
Specifier loop
Anti-terminator
5'-UCGUUU-3'
5'-UUUCUU-3'
3
GA-motif
Anti-terminator
sequence
T-box
5'-AUGGUA-3'
5'-A----A-3'
2
Stem II
T-box
Confirmation of
anti-terminator
b
WT
1
2
3
4
Methionine concentration (mM)
10
1
0.5
0.035
0.025
GFP (arbitrary units)
c
0.27 mM L-met